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| 09/647,027 | 02/09/2001 | Masaaki Muramatsu | 06501 064001 | 3825 |

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| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | 15 |

DATE MAILED: 08/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/647,027 | MURAMATSU ET AL. | |
| | Examiner | Art Unit | |
| | Ethan Whisenant, Ph.D. | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *7-10 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

## DETAILED ACTION

**1.** Applicant's election of Group I (Claims 1-6 and 11-13) without traverse in Paper No. 14 is acknowledged. Claims 7 and 14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. The restriction requirement has been reconsidered, is deemed proper and is therefore, herein made **FINAL**.

### SEQUENCE RULES

**2.** This application complies with the sequence rules and the sequences have been entered by the Scientific and Technical Information Center.

### 35 USC § 112- 2ND PARAGRAPH

**3.** The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

### CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

**4.** **Claim(s) 1-3** is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**Claim 1** is indefinite because there is no nexus between the preamble and the claim steps. Claim 1 in its preamble direct to a method which is to accomplish a particular goal. However, none of the claim steps states that this goal is accomplished. For clarity, claimed methods should recite that the purpose of the method has been attained (i.e. provide a nexus between the preamble and the claim steps).

**35 USC § 102**

**5.** The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

**CLAIM REJECTIONS UNDER 35 USC § 102**

**6.** **Claim(s) 1-6 and 11-13** is/are rejected under 35 U.S.C. 102(a) as being anticipated by Muramatsu et al. [WO9849282 (MAY 98)]

Muramatsu et al. teach a method comprising all of the limitations recited in Claims 1-6 and 11-13.

**35 USC § 103**

**7.** The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**8.** This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

**CLAIM REJECTIONS UNDER 35 USC § 103**

**9.** **Claim(s) 1-2, 11-12** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Banker et al. [US 5, 643,730 (1997)] in view of Schena (May 96).

**Claim 1** is drawn to a method for detecting changes in gene expression levels in cells treated with a particular compound which method comprises five steps. To begin, mRNA is isolated from treated and untreated cells. Then sets of cDNA from each mRNA sample are prepared by reverse transcription. The respective sets of cDNA are then labeled with different fluorescent labels. Next, each set of labeled cDNAs are hybridized to a probe DNA. Finally, differences in the amount of labeled cDNA hybridized to said probe DNA is detected via the color of the fluorescence emitted thereby allowing for the detection changes in gene expression levels in cells treated with a particular compound.

Banker et al. teach a method for detecting changes in gene expression levels in cells treated with a particular compound which comprises all of the limitations of Claim 1 except these authors do not explicitly teach differentially labeling the cDNA sets. However, the differential labeling of cDNA sets in gene expression analysis was well known at the time of the invention as evidenced by Schena. Note that Schena is a review article that teaches a two-color fluorescence detection scheme which allows for rapid and simultaneous differential expression analysis of independent biological samples and could, the author argues, also serve as a rapid method to identify changes in expression that accompany treatment of human cells with drugs or other compounds Therefore, absent an unexpected result it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to modify the method of Banker et al. wherein the two-color fluorescence detection scheme of Schena is utilized. Motivation for making this modification comes from Schena who teaches that his two-color fluorescence detection scheme allows for the rapid and simultaneous analysis of independent biological samples and can serve as a rapid method to identify changes in expression patterns following the treatment of human cells with drugs or other compounds. Also, note that Schena teaches that "unlike conventional methods the use of a single microarray for the measurement of differential expression avoids complications inherent in comparing the results from independent hybridizations".

**Claim 2** is drawn to an embodiment of Claim 1 wherein the labeled cDNAs are hybridized simultaneously to a large number of probe DNAs.

Schena teach this limitation. See, for example, Column 1 on page 428.

**Claim 4** is drawn to a method of screening for a gene whose expression level is altered by a particular compound. This method is to comprise six steps. To begin, mRNA is isolated from treated and untreated cells. Then sets of cDNA from each mRNA sample are prepared by reverse transcription. The respective sets of cDNA are then labeled with different fluorescent labels. Next, each set of labeled cDNAs are hybridized to a gene probe DNA. Then, differences in the amount of labeled cDNA hybridized

to said gene probe DNA is detected via the color of the fluorescence emitted, Finally, a gene probe which exhibits a differential pattern of hybridization with the two sets of differently labeled cDNAs is identified thereby identifying a gene whose expression level is altered by a particular compound.

Banker et al. teach a method of screening for a gene whose expression level is altered by a particular compound which comprises all of the limitations of Claim 1 – see, for example, the abstract - except these authors do not explicitly teach differentially labeling the cDNA sets. However, the differential labeling of cDNA sets in gene expression analysis was well known at the time of the invention as evidenced by Schena. Note that Schena is a review article that teaches a two-color fluorescence detection scheme which allows for rapid and simultaneous differential expression analysis of independent biological samples and could, the author argues, also serve as a rapid method to identify changes in expression that accompany treatment of human cells with drugs or other compounds Therefore, absent an unexpected result it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to modify the method of Banker et al. wherein the two-color fluorescence detection scheme of Schena is utilized. Motivation for making this modification comes from Schena who teaches that his two-color fluorescence detection scheme allows for the rapid and simultaneous analysis of independent biological samples and can serve as a rapid method to identify changes in expression patterns following the treatment of human cells with drugs or other compounds. Also, note that Schena teaches that "unlike conventional methods the use of a single microarray for the measurement of differential expression avoids complications inherent in comparing the results from independent hybridizations".

**Claim 5** is drawn to an embodiment of Claim 4 wherein the labeled cDNAs are hybridized simultaneously to a large number of probe DNAs.

**Claim 11** is drawn to a method of screening for a compound which alters the expression level of gene. This method is to comprise six steps. To begin, mRNA is isolated from treated and untreated cells. Then sets of cDNA from each mRNA sample are prepared by reverse transcription. The respective sets of cDNA are then labeled with different fluorescent labels. Next, each set of labeled cDNAs are hybridized to a gene probe DNA. Then, differences in the amount of labeled cDNA hybridized to said gene probe DNA is detected via the color of the fluorescence emitted, Finally, a gene probe which exhibits a differential pattern of hybridization with the two sets of differently labeled cDNAs is identified from this information a compound which caused the differential expression pattern is identified.

Banker et al. teach a method of screening for a compound which alters the expression level of gene which comprises all of the limitations of Claim 1 – see, for example, the abstract - except these authors do not explicitly teach differentially labeling the cDNA sets. However, the differential labeling of cDNA sets in gene expression analysis was well known at the time of the invention as evidenced by Schena. Note that Schena is a review article that teaches a two-color fluorescence detection scheme which allows for rapid and simultaneous differential expression analysis of independent biological

samples and could, the author argues, also serve as a rapid method to identify changes in expression that accompany treatment of human cells with drugs or other compounds Therefore, absent an unexpected result it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to modify the method of Banker et al. wherein the two-color fluorescence detection scheme of Schena is utilized. Motivation for making this modification comes from Schena who teaches that his two-color fluorescence detection scheme allows for the rapid and simultaneous analysis of independent biological samples and can serve as a rapid method to identify changes in expression patterns following the treatment of human cells with drugs or other compounds. Also, note that Schena teaches that "unlike conventional methods the use of a single microarray for the measurement of differential expression avoids complications inherent in comparing the results from independent hybridizations".

**Claim 12** is drawn to an embodiment of Claim 11 wherein the labeled cDNAs are hybridized simultaneously to a large number of probe DNAs.

Schena teach this limitation. See, for example, Column 1 on page 428.

**10.** **Claim(s) 3 and 13** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Banker et al. [US Patent No. 5, 643,730 (1997)] in view of Schena (May 96) as applied above and further in view of Lockhart et al. [US Patent No. 5, 643,730 (1997)].

**Claim 3** is drawn to an embodiment of Claim 1 wherein one cDNA set is labeled with rhodamine while the other cDNA is labeled with FITC. **Claim 6** is drawn to an embodiment of Claim 4 wherein one cDNA set is labeled with rhodamine while the other cDNA is labeled with FITC. **Claim 13** is drawn to an embodiment of Claim 11 wherein one cDNA set is labeled with rhodamine while the other cDNA is labeled with FITC.

Banker et al. in view of Schena teach all of the limitations of Claims 3, 6 and 13 except these authors do not explicitly teach using rhodamine – in combination with fluorescein - as one of the fluorescent labels, rather the combined teachings of Banker et al. in view of Schena suggest using FITC (i.e. fluorescein) in combination with lissamine. However, as evidenced by Lockhart et al. - see, for example, Column 13, last paragraph - rhodamine and the use of rhodamine in expression analysis was well known art the time of the invention. Therefore, absent an unexpected result it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to modify the method of Banker et al. in view of Schena wherein rhodamine in combination with fluorescein is used as one of the fluorescent labels instead of lissamine in combination with fluorescein. Absent an unexpected result, the substitution of one known reagent with well known properties for a second well known reagent with known properties is routine in the art. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected

functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

## CONCLUSION

**10.** **Claim(s) 1-6 and 11-13** is/are rejected and/or objected to for the reason(s) set forth above.

**11.** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (703) 308-6567. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

The fax number for this Examiner is (703) 746-8465. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989). Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.

ETHAN C. WHISENANT
PRIMARY EXAMINER